Qualification of the aseptic process for preparing 10%-5% glycerol-fructose bags

A. Megnounif, C. Baguet, P. Chapron, E. Olivier, N. Cormier (Pharmacie, Nantes Université, CHU Nantes, F-44000, Nantes)

COM25-56025

Introduction

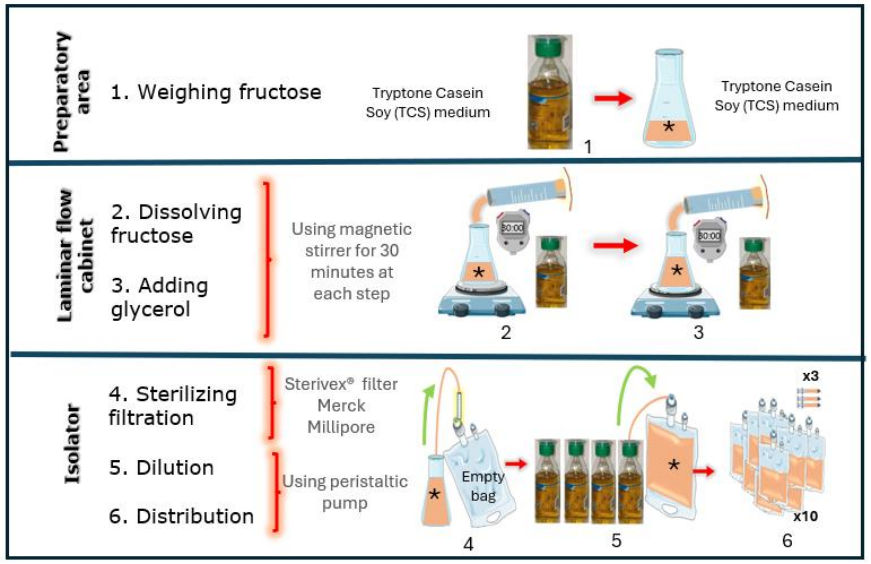
Colorectal polyps, although mostly benign, can develop into colorectal cancer and require endoscopic resection. In our center, a sterile 10%-5% glycerol-fructose solution, prepared from non-sterile raw materials, is injected into the submucosa to facilitate the procedure. Given its use as an injectable preparation, the solution must comply with strict sterility standards of the french GMPs.

The aim of this study

Validation of the aseptic process for the semi-automated preparation of sterile 10% glycerol – 5% fructose solution bags from non-sterile raw materials using a Media Fill Test (MFT).

Materials & methods

- **3 MFT** conducted by **3 operators** in **3 different time slots.**
- Batch of **10 bags (100 mL)** and **3 syringes (5 mL)** by each operator.
- **Unfavorable conditions**: no monthly cleaning of the isolator, no glove change after the sterilizing filtration step.

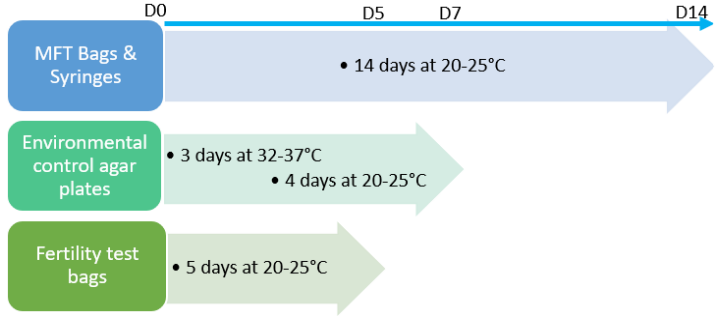


Simulation of preparation process steps through an MFT

- **Fertility test** performed on both filtered and non-filtered growth medium (TCS).
  - Positive controls: Inoculation of 3 bags of unfiltered broth.
  - Negative controls: 2 non-inoculated bags with filtered and unfiltered broth.
- **Incubation.**
- **Environmental monitoring** performed including air sedimentation agar plate, contact agar plates, and glove imprint agar plates (operator + assistant).

Bacillus subtilis
Candida albicans
Aspergillus brasiliensis

Microorganisms inoculated according to the recommendations of the European Pharmacopoeia



Incubation conditions

Results

- **Media fill test:**
  - No microbial growth observed in bags and syringes after 14 days of incubation.
  - No colonies detected on environmental monitoring plates over 7 days.
- **Fertility test:**
  - Microbial growth observed in all inoculated bags after 4–5 days.
  - Non-inoculated bags, whether filtered or not, remained clear.

Discussion & conclusion

Microbial growth in the inoculated bags confirms that the sterilizing filtration did not compromise the fertility of the broth.

The absence of microbial growth in the MFT bags and syringes, despite the use of non-sterile raw materials and multiple preparation steps, along with compliant environmental monitoring results, confirms the validation of the process.

Overall, these findings demonstrate that the preparation adheres to the strict sterility requirements of French GMP.

References

Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-operation Scheme, 25 August 2023, Annex 1 Manufacture of sterile medicinal products, Aseptic process simulation (APS) (also known as media fill), p54. - Guide to good manufacturing practice for medicinal products annexes : file:///C:/Users/0035FAB3/Downloads/pe-009-17-gmp-guide-xannexes.pdf - Bonnes pratiques de preparations, ANSM, Ed 2022, LD1: preparation de medicaments stériles, Préparation et conditionnement. - Marie-Caroline HUSSON, Polypes colorectaux : intérêt de la solution fructose-glycérine. Dossier du CNHIM, 2021, XLII, 2 - 4. - Tall ML, Salmon D, Diouf E, Drai J, Filali S, Lépilliez V, et al. Aseptic process validation and stability study of an injectable preparation of fructose (5%)—glycerol (10%) as part of a hospital clinical research program on endoscopic curative treatment for early epithelial neoplastic lesions of the gastrointestinal tract. Annales Pharmaceutiques Françaises [Internet]. 5 septembre 2014 - European Pharmacopoeia 11th Ed, General Chapter 2.6.1. Sterility test.